Urinary Retention as a Rare Adverse Effect of Clozapine

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Urinary incontinence can have a negative influence on a patient's quality of life and cause noncompliance with medication adherence. Urinary retention can lead to irritability and agitation, requiring emergency treatment. This case report describes rare adverse effects of clozapine in a patient who had been managed on this medication for a few years.

Case Report

A 65-year-old man with a past psychiatric diagnosis of intellectual disability, autism spectrum disorder, and schizophrenia presented to the emergency department from his group home due to agitation and aggressive behavior with active visual hallucinations. The patient was prescribed risperidone and topiramate in the past but was noncompliant. He was known to be nonverbal at baseline but was observed occasionally grunting and lashing out at caregivers. He had no history of urinary retention or incontinence.

Risperidone was restarted with no significant improvement in his condition. His medication was changed to clozapine and titrated to an effective dose of 200 mg twice/d. The patient continued to have frequent physical outbursts and agitation in the inpatient unit, and valproate and topiramate were eventually added to augment mood stabilization. On the third day after introducing clozapine, the patient was noted to have decreased urinary output with progressively increasing lower abdominal pain. Additionally, to relieve anxiety, clonazepam was added to his medications.

With all these medication changes and given his intellectual disability diagnosis, the patient was at risk of falls and reactive aggression, for which a one-on-one sitter was present at all times. His oral intake continued to be very poor, and he developed ketonuria. The total score of the Adverse Drug Reaction Probability Scale[1] was 8. On medical evaluation, he was also found to have trace pleural effusion at his left lung base, and he was transferred to the medical floor due to poor oral intake. The patient required a nasogastric tube to address his nutrition needs and straight catheterization for worsening urinary retention.

The psychiatric consultation team followed up with the patient on the medical floor and decided to lower the dose of clozapine, which caused a decrease in urinary retention after 4 to 5 days. He showed improvement in his behavior and was at his baseline level on clozapine 25 mg twice/d, valproate and topiramate for mood stabilization, and tamsulosin for urinary retention.

Discussion

Clozapine is an atypical antipsychotic indicated in the management of treatment-resistant schizophrenia. Clozapine binds dopamine receptors and exerts potent anticholinergic, adrenolytic, antihistaminic, and serotoninergic activity. Patients treated with clozapine may experience adverse effects, ranging in severity from relatively benign to serious and potentially life-threatening conditions such as seizures and agranulocytosis.

Several possible mechanisms can explain the occurrence of urinary retention and incontinence. The potent anticholinergic activity of clozapine may result in urinary retention with subsequent overflow resulting in incontinence. It has also been proposed that the antiadrenergic activity of clozapine decreases bladder sphincter tone and causes bladder emptying. Clozapine can cause an overactive bladder tone, resulting in continuous impairment due to acting as a dopamine antagonist. Clozapine-induced constipation may aggravate urinary retention, resulting in secondary overflow, and incontinence secondary to diabetes and seizures may also occur.[2,3] Another mechanism often considered is the sedating property of clozapine, which reduces the urge of micturition, causing retention that sometimes leads to overflow.[4] Some studies[5] have shown that clozapine has a high probability of causing drug-induced diabetes insipidus in some patients, which causes polyuria. With the contribution of various other mechanisms, as reported here, urinary retention is seen.[5]

Conclusions

This case suggests the importance of understanding the rare but known anticholinergic side effect of clozapine, which has been shown to adversely influence bladder control. Resolution of urinary incontinence at a lower dose of clozapine suggests the importance of careful medication monitoring.

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